

AGGTTCGACGGCGGGCGTGGCTGGAGCGGGGGCCGCGGCCGCGCCGACAGAGATGTGACTCGGGCCGAAGGC
 CAGCTGGAGCGTCGGCGCTGCGGGGCCGCGGGGGTCAATGTTTCGTGGCATCAGAGAGAAAGATGAGAGC
 TCACCAGGTGCTCACCTTCCTCCTGCTCTTCGTGATCACCTCGGTGGCCTCTGAAAACGCCAGCACATCC
 CGAGGCTGTGGGCTGGACCTCCTCCCTCAGTACGTGTCCCTGTGCGACCTGGACGCCATCTGGGGCATTG
 TGGTGGAGGCGGTGGCCGGGGCGGGCGCCCTGATCACACTGCTCCTGATGCTCATCCTCCTGGTGGCGCT
 GCCCTTCATCAAGGAGAAGGAGAAGAAGAGCCCTGTGGGCCTCCACTTCTGTTTCTCCTGGGGACCCTG
 GGCCTCTTTGGGCTGACGTTTGCTTCATCATCCAGGAGGACGAGACCATCTGCTCTGTCCGCCGCTTCC
 TCTGGGGCGTCTCTTTGCGCTCTGCTTCTCCTGCCTGCTGAGCCAGGCATGGCGCGTGGCGAGGCTGGT
 GCGGCATGGCACGGGGCCCCGCGGGCTGGCAGCTGGTGGGCCTGGCGCTGTGCCTGATGCTGGTGCAAGTC
 ATCATCGCTGTGGAGTGGCTGGTGCTCACCGTGCTGCGTGACACAAGGCCAGCCTGCGCCTACGAGCCCA
 TGGACTTTGTGATGGCCCTCATCTACGACATGGTACTGCTTGTGGTCACCCTGGGGCTGGCCCTCTTCAC
 TCTGTGCGGCAAGTTCAAGAGGTGGAAGCTGAACGGGGCCTTCTCCTCATCACAGCCTTCTCTCTGTG
 CTCATCTGGGTGGCCTGGATGACCATGTACCTCTTCGGCAATGTCAAGCTGCAGCAGGGGGATGCCTGGA
 ACGACCCACCTTGGCCATCACGCTGGCGGCCAGCGGTGGGTCTTCGTCTATCTTCCACGCCATCCCTGA
 GATCCACTGCACCCTTCTGCCAGCCCTGCAGGAGAACACGCCCACTACTTCGACACGTGCGAGCCAGG
 ATGCGGGAGACGGCCTTCGAGGAGGACGTGCAGCTGCCGCGGGCCTATATGGAGAACAAGGCCTTCTCCA
 TGGATGAACACAATGCAGCTCTCCGAACAGCAGGATTTCCCAACGGCAGCTTGGGAAAAAGACCCAGTGG
 CAGCTTGGGGAAAAGACCCAGCGCTCCGTTTAGAAGCAACGTGTATCAGCCAACCTGAGATGGCCGTCGTG
 CTCAACGGTGGGACCATCCCAACTGCTCCGCCAAGTCACACAGGAAGACACCTTTGGTGAAAGACTTTAA
 GTTCCAGAGAATCAGAATTTCTCTTACCGATTTGCCCTCCCTGGCTGTGTCTTTCTTGAGGGAGAAATCGG
 TAACAGTTGCCGAACCAGGCCGCTCACAGCCAGGAAATTTGGAAATCCTAGCCAAGGGGATTTCTGTGTA
 AATGTGAACACTGACGAACTGAAAAGCTAACACCGACTGCCCGCCCCCTCCCCTGCCACACACACAGACAC
 GTAATACCAGACCAACCTCAATCCCCGAAACTAAAGCAAAGCTAATTGCAAATAGTATTAGGCTCACTG
 GAAAATGTGGCTGGGAAGACTGTTTCATCCTCTGGGGGTAGAACAGAACCAATTCACAGCTGGTGGGCC
 AGACTGGTGTTGGTTGGAGGTGGGGGGCTCCCACTCTTATCACCTCTCCCCAGCAAGTGCTGGACCCAG
 GTAGCCTCTTGGAGATGACCGTTGCGTTGAGGACAAATGGGGACTTTGCCACCGGCTTGCCTGGTGGTTT
 GCACATTTACAGGGGGGTCAGGAGAGTTAAGGAGGTTGTGGGTGGGATTCCAAGGTGAGGCCCAACTGAAT
 CGTGGGGTGAGCTTTATAGCCAGTAGAGGTGGAGGGACCCTGGCATGTGCCAAAGAAGAGGCCCTCTGGG
 TGATGAAGTGACCATCACATTTGGAAAGTGATCAACCACTGTTTCCTTCTATGGGGCTCTTGCTCTAATGT
 CTATGGTGAGAACACAGGCCCCGCCCTTCCCTTGTAGAGCCATAGAAATATTCTGGCTTGGGGCAGCAG
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 TTATTCCCTTATTCAATTTCAAGAGCTCCAATGGGGTCTCCAGCTGAAAGCCCCCTCCGGGAGGCAGGTTGG
 AAGGCAGGCACCACGGCAGGTTTTCCGCGATGATGTACCTAGCAGGGCTTCAGGGGTTCCCACTAGGAT
 GCAGAGATGACCTCTCGCTGCCTACAAGCAGTGACACCTCGGGTCCTTTCCGTTGCTATGGTGAAAATT
 CCTGGATGGAATGGATCACATGAGGGTTTCTTGTTGCTTTTGGAGGGTGTGGGGGATATTTTGTTTTGGT
 TTTTCTGCAGGTTCCATGAAAACAGCCCTTTTCCAAGCCCATTGTTTCTGTCTATGGTTTCCATCTGTCTT
 GAGCAAGTCATTCCTTTGTTATTTAGCATTTCGAACATCTCGGCCATTCAAAGCCCCCATGTTCTCTGCA
 CTGTTTGGCCAGCATAACCTCTAGCATCGATTCAAAGCAGAGTTTTAACCTGACGGCATGGAATGTATAA
 ATGAGGGTGGGTCTTCTGCAGATACTCTAATCACTACATTGCTTTTTTCTATAAACTACCCATAAGCCT
 TTAACCTTTAAAGAAAAATGAAAAAGGTTAGTGTTTGGGGGCCGGGGGAGGACTGACCGCTTCATAAGCC
 AGTACGTCTGAGCTGAGTATGTTTCAATAAACCTTTTGATATTTCTCAAAAAAAAAAAAAAAAAAAAAA
 (SEQ ID NO:1)

FIGURE 1A

MFVASERKMRAHQVLTFLLLFVITSVASENASTSRGCGLDLLPQYVSLCDLDAIWGIVVEAVAG
AGALITLLLMLILLVRLPFIKEKEKKSPVGLHFLFLLGTLGLFGLTFAFIIQEDETICSVRRFL
WGVLFALCFSCLLSQAWRVRLVRHGTGPAGWQLVGLALCLMLVQVIIAVEWLVLTVLRDTRPA
CAYEPMDFVMALIYDMVLLVVTGLGLALFTLCGKFKRWKLNGAFLITAFLSVLIWVAWMTMYLF
GNVKLQQGDAWNDPTLAITLAASGWVFVIFHAIPEIHCTLLPALQENTPNYFDTSQPRMRETAF
EEDVQLPRAYMENKAFSMDEHNAALRTAGFPNGSLGKRPSGSLGKRPSAPFRSNVYQPTEMAVV
LNGGTIPTAPPSHTGRHLW (SEQ ID NO:2)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGGTGCGAGGCGGGCGTGGCTGGAGCGGGGGCCGCGGCCGCGCCGAGAGATGTGACTCG
 GGCCGAAGGCCAGCTGGAGCGTCGGCGCTGCGGGGCCGCGGGGGTTCGAATGTTTCGTGGCA
 TCAGAGAGAAAGATGAGAGCTCACCAGGTGCTCACCTTCTCCTGCTCTTCGTGATCACC
 TCGGTGGCCTCTGAAAACGCCAGCACATCCCAGGCTGTGGGCTGGACCTCCTCCCTCAG
 TACGTGTCCCTGTGCGACCTGGACGCCATCTGGGGCATTGTGGTGGAGGCGGTGGCCGGG
 GCGGGCGCCCTGATCACACTGCTCCTGATGCTCATCTCCTGGTGGGCTGCCCTTCATC
 AAGGAGAAGGAGAAGAAGAGCCCTGTGGGCTCCACTTTCGTTCCTCCTGGGGACCTTG
 GGCTCTTTGGGCTGACGTTTGCCTTCATCATCCAGGAGGACGAGACCATCTGCTCTGTC
 CGCCGCTTCTCTGGGGCGTCTCTTTGCGCTCTGCTTCTCCTGCTGCTGAGCCAGGCA
 TGGCGCGTGGGAGGCTGGTGGCGCATGGCACGGGCCCGCGGGCTGGCAGCTGGTGGGC
 CTGGCGCTGTGCTGATGCTGGTGCAAGTCATCATCGCTGTGGAGTGGCTGGTGGCTCACC
 GTGCTGCGTGACACAAGGCCAGCCTGCGCCTACGAGCCCATGGACTTTGTGATGGCCCTC
 ATCTACGACATGGTACTGCTTGTGGTCACCCTGGGGCTGGCCCTCTTCACTCTGTGCGGC
 AAGTTCAAGAGGTGGAAGCTGAACGGGGCCTTCTCCTCATCACAGCCTTCTCTCTGTG
 CTCATCTGGGTGGCCTGGATGACCATGTACCTCTTCGGCAATGTCAAGCTGCAGCAGGGG
 GATGCCCTGGAACGACCCACCTTGGCCATCACGCTGGCGGCCAGCGGCTGGGTCTTCGTC
 ATCTTCCACGCCATCCCTGAGATCCACTGCACCCTTCTGCCAGCCCTGCAGGAGAACACG
 CCCAACTACTTCGACACGTCGCAGCCAGGATGCGGGAGACGGCCTTCGAGGAGGACGTG
 CAGCTGCCCGGGCCTATATGGAGAACAAGGCCTTCTCCATGGATGAACACAATGCAGCT
 CTCCGAACAGCAGGATTTCCCAACGGCAGCTTGGGAAAAAGACCCAGTGGCAGCTTGGGG
 AAAAGACCCAGCGCTCCGTTTAGAAGCAACGTGTATCAGCCAACTGAGATGGCCGCTCGTG
 CTCAACGGTGGGACCATCCCAACTGCTCCGCCAAGTCACACAGGAAGACACCTTTGGTGA
 AAGACTTTAAGTTCCAGAGAATCAGAATTTCTCTTACCGATTTGCCCTCCCTGGCTGTGTC
 TTTCTTGAGGGAGAAATCGGTACAGTTGCCGAACCAGGCCGCTCACAGCCAGGAAATTT
 TGGAAATCCTAGCCAAGGGGATTTCTGTGTAATGTGAACACTGACGAACTGAAAAGCTAA
 CACCGACTGCCCGCCCCCTCCCTGCCACACACAGACACGTAATACCAGACCAACCTCA
 ATCCCCGCAAACTAAAGCAAGCTAATTGCAAAATAGTATTAGGCTCACTGGAAAATGTGG
 CTGGGAAGACTGTTTCATCTCTGGGGGTAGAACAGAACCAAAATTCACAGCTGGTGGGCC
 AGACTGGTGTGTTGGTGGAGGTGGGGGGCTCCCACTTATCACCTCTCCCCAGCAAGTGC
 TGGACCCAGGTAGCCTCTTGGAGATGACCGTTGCGTTGAGGACAAATGGGGACTTTGCC
 ACCGGCTTGCTGGTGGTGGTTCACATTTACGGGGGGTCAGGAGAGTTAAGGAGGTGTGG
 GTGGGATTCCAAGGTGAGGCCAACTGAATCGTGGGGTGAGCTTTATAGCCAGTAGAGGT
 GGAGGGACCTGGCATGTGCCAAAGAAGAGGCCCTCTGGGTGATGAAGTGACCATCACAT
 TTGGAAAGTGATCAACCACTGTTCCTTCTATGGGGCTCTTGCTCTAATGTCTATGGTGAG
 AACACAGGCCCCGCCCCCTCCCTTGTAGAGCCATAGAAATATTCTGGCTTGGGGCAGCAG
 TCCCTTCTTCCCTTGATCATCTCGCCCTGTTCTTACACTTACGGGTGTATCTCCAAATCC
 TCTCCCAATTTTATTCCCTTATTCAATTTCAAGAGCTCCAATGGGGTCTCCAGCTGAAAGC
 CCTCCGGGAGGCAGGTGGGAAGGCAGGCACCACGGCAGGTTTCCGCGATGATGTCACC
 TAGCAGGGCTTCAGGGGTTCCTACTAGGATGCAGAGATGACCTCTCGCTGCCTCACAAGC
 AGTGACACCTCGGGTCCCTTCCGTTGCTATGGTGAAAATTCCTGGATGGAATGGATCACA
 TGAGGGTTTCTTGTGCTTTTGGAGGGTGTGGGGGATATTTTGTTTTGGTTTTCTGCAG
 GTTCCATGAAAACAGCCCTTTTCCAAGCCATTGTTTCTGTCATGGTTCCATCTGTCCT
 GAGCAAGTCATTCCTTTGTTATTAGCATTTTGAACATCTCGGCCATTCAAAGCCCCCAT
 GTTCTCTGCACTGTTTGGCCAGCATAACCTCTAGCATCGATTCAAAGCAGAGTTTAAACC
 TGACGGCATGGAATGTATAAATGAGGGTGGGTCTTCTGCAGATACTCTAATCACTACAT
 TGCTTTTCTATAAACTACCCATAAGCCTTTAACCTTTAAAGAAAAATGAAAAAGGTTA
 GTGTTTGGGGGCCGGGGAGGACTGACCGCTTCATAAGCCAGTACGCTGAGCTGAGTAT
 GTTCAATAAACCTTTTGATATTCTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 2A

Gene Sequence Structure *

526 bp

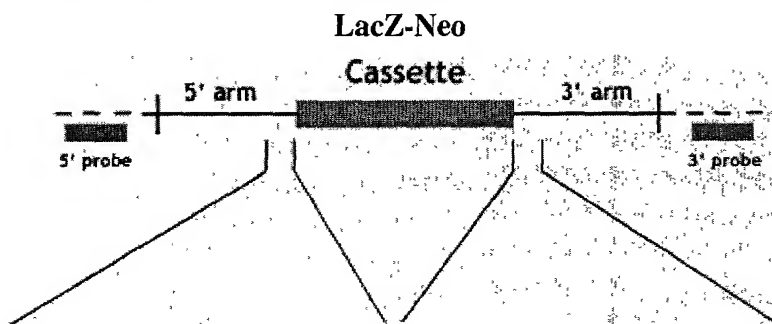
Sequence Deleted

594 bp

Size of full-length
cDNA: 2870 bp

Targeting Vector* (genomic sequence)

Arm Length:
5': 4.2 kb
3': 0.7 kb



— Targeting Vector
- - - Endogenous Locus

* Not drawn to scale

5' >TGATGCTCATTCTCCTAGTGA
GACTACCCTTCATCAAGGACAAGG
AAAGGAAGCGGCTGTGTGCCTCC
ATTTCTCTTCCTGCTGGGGACCC
TGGGCCCTCTTTGGCCTGACGTTTG
CCTTCATCATCCAGATGGACGAGA
CAATCTGCTCCATCCGACGCTTCC
TCTGGGGTGTCTCTTCGCGCTCT
GCTTTTCCGCT<3' (SEQ ID
NO:3)

5' >GTGAGCCTGGCACTGTGCCTG
ATGCTGGTGCAGGTCATCATTGCC
ACTGAGTGGCTGGTGCTGACTGTG
CTGCGTGACACGAAGCCAGCCTGC
GCCTACGAGCCCATGGATTTTGTG
ATGGCGCTCATCTACGACATGGTG
CTGCTGGCCATCACCTGGCCCAG
TCCCTCTTCACGCTGTGTGGCAAG
TTCAAACGGTG<3' (SEQ ID
NO:4)

FIGURE 2B

